selection" (species IB) and "identification of a polypeptide with quantitation of the polypeptide" (Species IIB).

Regarding the Objections

Regarding the objection to the drawings, submitted herewith are formal drawings that address the objections raised by the draftsman. Accordingly, Applicant respectfully requests that this objection to the drawings be withdrawn.

Regarding the objection to claim 12, claim 12 has been amended to depend from claim 2. Therefore, this objection has been rendered moot, and Applicant respectfully requests that this objection be withdrawn.

Double Patenting Rejection

The provisional rejection of claims 1-5, 8-16, 18-23 and 37-47 under the judicially created doctrine of obviousnees-type double patenting as allegedly unpatentable over claims 1-23 and 32-43 of co-pending application serial No. 09/748,793 is respectfully traversed. Applicant submits that the claims of the co-pending applications are patentably distinct. The claims of co-pending application serial No. 09/748,793 are not directed to simultaneously determining the mass of a subset of parent polypeptides from a population of polypeptides and the mass of fragments of the subset of parent polypeptides. Therefore, Applicant submits that the present claims are unobvious over

serial No. 09/748,793 and respectfully requests that this provisional double patenting rejection be withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 1-23 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite is respectfully traversed. Claims 7-11 and 18-22 have been amended to indicate that the mass of the parent polypeptides and fragments is determined at a specifically recited mass accuracy. Applicant submits that the claims are clear and definite and respectfully requests that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 102

The rejection of claims 1, 2, 4-12, 24, 25, 27-38, and 40-47 under 35 U.S.C. § 102(b) as allegedly anticipated by Bruce et al., Anal. Chem. 71:2595-2599 (1999), is respectfully traversed. Applicant respectfully submits that the claims are novel over Bruce et al.

With regard to claims 1 and 13, these claims are directed to methods of identifying a polypeptide that include the step of simultaneously determining the mass of a subset of parent polypeptides from a population of polypeptides and the mass of fragments of the subset of parent polypeptides. In contrast to the claimed methods, Bruce et al. does not teach simultaneously determining the mass of a subset of parent polypeptides from a population of polypeptides and the mass of fragments of the

subset of parent polypeptides. With regard to the reference in the Office Action of the description in Bruce et al. of FTICR-MS providing "the highest combination of simultaneous mass measurement accuracy, resolution and sensitivity," Applicant points out that the reference to "simultaneous" does not refer to simultaneously determining the mass of a subset of parent polypeptides from a population of polypeptides and the mass of fragments of the subset of parent polypeptides, as in Applicant's claimed methods.

Furthermore, Bruce et al. does not teach the use of an "annotated polypeptide index," as recited in the claims. The specification teaches that an annotated polypeptide index refers to a polypeptide identification index comprising at least one empirically determined characteristic for each of the polypeptides in the index (page 19, line 28, to page 20, line 8). In contrast, Bruce et al. does not teach the use of an annotated polypeptide index. Bruce et al. describes using an algorithm to compare the resulting masses to a "generated table of masses based on all possible proteolysis products for the protein" (page 2597, left column, lines 6-8). Bruce et al. further describes that the "program presents as output a table of the experimentally measured masses and the predicted polypeptides (if any) that fall within the search criteria established by the user" (page 2597, lines 16-19; emphasis added). Thus, the database described in Bruce et al. for comparison of experimentally determined masses is a database based on predicted masses and is not a database comprising at least one empirically determined characteristic for each polypeptide in the index.

Accordingly, Bruce et al. cannot anticipate claims reciting an annotated polypeptide index.

Regarding claims 6, 17 and 24, these claims recite that the fragment mass is determined by mass spectrometry in the absence of ion selection for producing fragment ions. In contrast, Bruce et al. does not teach mass determination in the absence of ion selection. Absent such a teaching, Bruce et al. cannot anticipate these claims.

Regarding claim 37, this claim recites that the fragment mass is determined by mass spectrometry at an accuracy in ppm of greater than 2.5 ppm. In contrast, Bruce et al. does not teach determining fragment mass at an accuracy of greater than 2.5 ppm. Therefore, Bruce et al. cannot anticipate claim 37 and its dependent claims.

As discussed above, Bruce et al. does not teach Applicant's claimed methods. Accordingly, Applicant submits that the claimed methods are novel over Bruce et al. and respectfully requests that this rejection be withdrawn.

The rejection of claims 1-10, 12-21, 23-31, 33-42, and 44-47 under 35 U.S.C. § 102(a) as allegedly anticipated by Goodlett et al., Anal. Chem. 72:1112-1118 (2000), is respectfully traversed. Applicant submits that the claimed methods are novel over Goodlett et al.

In contrast to the claimed methods, Goodlett et al. does not teach simultaneously determining the mass of a subset of parent polypeptides from a population of polypeptides and the mass of fragments of the subset of parent polypeptides. Furthermore, Goodlett et al. does not teach determining the fragment mass in the absence of ion selection. Therefore, Goodlett et al. cannot anticipate the claims.

In regard to the description in Goodlett et al. on page 1113, column 1, lines 11-22, referred to in the Office Action, this description is directed to describing the disadvantage of collision-induced dissociation (CID) requiring sequential selection of peptide ions and the difficulties of analyzing lower intensity peptide ions in complex peptide mixtures. However, this description does not teach absence of ion selection. Furthermore, Applicant respectfully disagrees with the assertion in the Office Action on page 8 that "[T]his absence of ion selection criteria is then applied to the experiment with varying mass accuracies, ranging from 0.1 ppm to 10.0 ppm (Figure 1)." Figure 1 does not reflect "absence of ion selection criteria." Figure 1 shows all possible unique peptide molecular weights after digestion of all yeast proteins in the National Center for Biotechnology Information at a mass accuracy of 0.1, 1.0 and 10.0 ppm. This figure represents the calculated percentage of unique peptide molecular weights based on the theoretical tryptic digest of all yeast proteins available in the NCBI database and does not represent the determination of fragment mass by mass spectrometry in the absence of ion selection for producing fragment ions, as in Applicant's claims.

With regard to claim 37, Goodlett does not teach determining fragment mass at an accuracy of greater than 2.5 ppm. At best, Goodlett et al. describes acquiring mass spectra using electrospray ionization-Fourier transform ion cyclotron resonance mass spectrometry (ESI-FTICR MS) at a higher mass accuracy (lower ppm) of 1 ppm (page 1113, second column, last complete sentence). Therefore, Goodlett et al. cannot anticipate this claim.

As discussed above, Goodlett et al. does not teach Applicant's claimed methods. Accordingly, Applicant submits that the claimed methods are novel over Goodlett et al. and respectfully requests that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 103

The rejection of claims 1-47 under 35 U.S.C. § 103 as allegedly obvious over Bruce et al., *supra*, in view of Gygi et al., Nat. Biotechnol. 17:994-999 (1999), is respectfully traversed. Applicant respectfully submits that the claimed methods are unobvious over Bruce et al., alone or in combination with Gygi et al.

For the reasons described above, Bruce et al. does not teach or suggest Applicant's claimed methods. In particular, Bruce et al. does not teach or suggest simultaneously determining the mass of a subset of parent polypeptides from a population of polypeptides and the mass of fragments of the subset of parent polypeptides. In addition, Bruce et al. does not teach or suggest the use of an annotated polypeptide index. Also, Bruce

et al. does not teach or suggest mass determination in the absence of ion selection. Furthermore, Bruce et al. does not teach or suggest determining fragment mass at an accuracy of greater than 2.5 ppm. Therefore, the claimed methods are unobvious over Bruce et al.

Gygi et al. does not cure the deficiencies of Bruce et al. Gygi et al. does not teach or suggest simultaneously determining the mass of a subset of parent polypeptides from a population of polypeptides and the mass of fragments of the subset of parent polypeptides, the use of an annotated polypeptide index, mass determination in the absence of ion selection, or determining fragment mass at an accuracy of greater than 2.5 ppm. Accordingly, Bruce et al., alone or in combination with Gygi et al., does not teach or suggest Applicant's claimed methods. Therefore, the claimed methods are unobvious over the cited references, and Applicant respectfully requests that this rejection be withdrawn.

The rejection of claims 1-47 under 35 U.S.C. § 103 as allegedly obvious over Bruce et al., *supra*, in view of Goodlett et al., *supra*, is respectfully traversed.

For the reasons described above, Bruce et al. does not teach or suggest Applicant's claimed methods. In particular, Bruce et al. does not teach or suggest simultaneously determining the mass of a subset of parent polypeptides from a population of polypeptides and the mass of fragments of the subset of parent polypeptides. In addition, Bruce et al. does not teach or

suggest the use of an annotated polypeptide index. Also, Bruce et al. does not teach or suggest mass determination in the absence of ion selection. Furthermore, Bruce et al. does not teach or suggest determining fragment mass at an accuracy of greater than 2.5 ppm. Therefore, the claimed methods are unobvious over Bruce et al.

Moreover, Goodlett et al. does not cure the deficiencies of Bruce et al. As discussed above, Goodlett et al. does not teach or suggest simultaneously determining the mass of a subset of parent polypeptides from a population of polypeptides and the mass of fragments of the subset of parent polypeptides, the use of an annotated polypeptide index, mass determination in the absence of ion selection, or determining fragment mass at an accuracy of greater than 2.5 ppm. Accordingly, Bruce et al., alone or in combination with Goodlett et al., does not teach or suggest Applicant's claimed methods. Therefore, the claimed methods are unobvious over the cited references, and Applicant respectfully requests that this rejection be withdrawn.

CONCLUSION

In light of the amendments and remarks herein, Applicant submits that the claims are now in condition for allowance and respectfully requests a notice to this effect. The

Examiner is invited to call the undersigned agent or Cathryn Campbell if there are any questions.

Respectfully submitted,

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APPENDIX A

7. (Amended) The method of claim 1, wherein **[said fragment]** **the** mass **of said parent polypeptides and fragments** is determined at an accuracy in ppm of greater than 1 ppm.

8. (Amended) The method of claim 1, wherein **[said fragment]** **the** mass **of said parent polypeptides and fragments** is determined at an accuracy in ppm of 2.5 ppm or greater ppm.

9. (Amended) The method of claim 1, wherein **[said fragment]** **the** mass **of said parent polypeptides and fragments** is determined at an accuracy in ppm of 5 ppm or greater ppm.

10. (Amended) The method of claim 1, wherein **[said fragment]** **the** mass **of said parent polypeptides and fragments** is determined at an accuracy in ppm of 10 ppm or greater ppm.

11. (Amended) The method of claim 1, wherein **[said fragment]** **the** mass **of said parent polypeptides and fragments** is determined at an accuracy in ppm of 100 ppm or greater ppm.

12. (Amended) The method of claim **[13]** **2**, wherein said characteristics are selected from the group consisting of polypeptide mass, amino acid composition, pI, and order of elution on a chromatographic medium.

18. (Amended) The method of claim 13, wherein **[said fragment]** **the** mass **of said parent polypeptides and fragments** is determined at an accuracy in ppm of greater than 1 ppm.

19. (Amended) The method of claim 13, wherein **[said fragment]** **the** mass **of said parent polypeptides and fragments** is determined at an accuracy in ppm of 2.5 ppm or greater ppm.

20. (Amended) The method of claim 13, wherein **[said fragment]** **the** mass **of said parent polypeptides and fragments** is determined at an accuracy in ppm of 5 ppm or greater ppm.

21. (Amended) The method of claim 13, wherein **[said fragment]** **the** mass **of said parent polypeptides and fragments** is determined at an accuracy in ppm of 10 ppm or greater ppm.

22. (Amended) The method of claim 13, wherein **[said fragment]** **the** mass **of said parent polypeptides and fragments** is determined at an accuracy in ppm of 100 ppm or greater ppm.